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BOUNCE

Predicting Effective Adaptation to Breast Cancer to Help Women to BOUNCE Back

Research and Innovation Action

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0. Document Info

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1. Introduction

This deliverable task (D2.3) describes the benefits of resilience following the conceptual work in task 2.1 and task 2.2. The aim of the BOUNCE project is to construct a measurement model of patient resilience to the physical and emotional challenges associated with breast cancer and with the burden incurred by associated treatments using data from the multi-center clinical pilot. The objectives of the project are: (1) to construct a conceptual model of multi-scale factors affecting individual resilience trajectories through diagnosis and treatments for breast cancer; (2) to identify expected personal or social and financial benefits of increased resilience in women recovering from breast cancer; (3) to address long-standing issues in the field of psycho-oncology regarding the dynamics of time-varying relationships between determinants of resilience and disease outcomes; and (4) to build a decision support tool that will be used in routine clinical practice in order to provide physicians and other health professionals with concrete, personalized recommendations regarding optimal psychosocial support strategies.

The purpose of WP2 is to (a) to delineate the evolution of resilience definition and to clarify the various ways this definition is conceptualized. In task 2.1 and task 2.2 a working definition for relicense was developed. Taken together and based on the literature review, our suggestion for working definition of resilience for BOUNCE - in the context of coping with breast cancer - is the following: *Resilience is a conglomerate of dynamic self-regulatory capacities that allow to mobilize and use internal and external resources over time in the face of adversity in order to maintain or promote well-being. The construct of resilience is used in three ways: (a) Resilience as a personal capacity or potential; (b) Resilience as an adaptive coping process or change trajectory; (c) Resilience as an outcome of maintaining healthy functioning and subjective well-being despite exposure to adversity. All these three aspects need to be measured.*

In task 2.3 we have conceptualized the tentative benefits of resilience and respond to the second BOUNCE overall objective (2) to identify expected personal, social and financial benefits of increased resilience in women recovering from breast cancer. The work in task 2.3 is primarily conceptual, and is based on a comprehensive literature review on the previously identified benefits of enhanced resilience for patients and the society. The work also presents the understanding from BOUNCE stakeholders on the benefits of resilience based on interviews conducted in collaboration with WP1 and WP8. The work further continues in BOUNCE WP7 where a cost and benefit model considering the benefits of resilience from a more quantitative perspective is created.

The work presented in task 2.3 and in this deliverable is fourfold:

1) Background literature on the benefits of resilience
2) Analysis of the stakeholders understanding of the benefits of resilience
3) Review on evidence-based resilience interventions
4) A preliminary quantitative analysis on the benefits of increased resilience for individuals and the society

2. Benefits of resilience for cancer patients

As presented in d2.1 and 2.2, there are multiple, sometimes unexpected, pathways to resilience (Mohlin et al. 2021). Resilience has been identified as an important aspect in coping with any kind of disease or trauma and there is a growing recognition that resilience to life-threatening situations, like cancer, might influence the overall impact of the treatment Bonanno et al., 2004). Factors that influence resilience have been identified in d2.1 and 2.2 as are biological factors (e.g., gene–environment interactions) (Kalisch et al., 2015), individuals' personal factors (e.g., self-efficacy, coping, optimism, and hope) (Hu et al 2015), and environmental factors, particularly social support (Somasundaram et al, 2016), collectively account to their resilience and psychological adaptations to the cancer experience (Eicher et al 2015). As also identified in d2.1 and 2.2 the experience of cancer a patient might also find benefits and personal growth. The influencing factors on resilience were identified in d2.1 and 2.1 and in this deliverable the aim has been to identify the possible benefit of resilience, both the strengthening and increasing theory.

The benefits of resilience have been previously analysed in several studies with the focus on better patient wellbeing as the main outcome. As pointed out in d2.1 and d2.2 although substantial distress can be associated with a cancer diagnosis and its treatment, many cancer patients show resilience and relatively maintain a stable quality of life (Carver, 1998; Gouzman et al., 2015, Ye et al., 2018). Furthermore, Mohlin et al. (2021) have recently found that higher levels of resilience are associated with higher levels of health-related quality of life (HRQoL) in breast cancer (BC) patients. However, not everyone reacts to a cancer diagnosis and cancer treatment in the same way, with some patients show decrease in their quality of life (Chan et al., 2006) and others may improve their quality of life over time (Lam et al., 2012). Learning more on the various trajectories of resilience and quality of life after the diagnosis of BC hold important clinical implications (Selier and Jenewein, 2019).

2.1 Resilience and mental health outcomes

A recently published literature review (Selier and Jenewein, 2019) found 154 published articles on the subject of benefits of strengthening resilience. The structured literature review searched studies related to benefits of resilience for cancer patients explored the relationships between resilience and mental health outcomes as well as discussed, the impact of resilience on the process of recovery from the disease, such as the clinical implications of this impact. Seiler and Jenewein (2019) conducted key word search in PubMed, with key words: cancer, cancer patients, cancer survivors, resilience, posttraumatic growth, coping, social support, and distress. In summary from the literature review a growing body of literature has linked resilience, in both cancer patients and cancer survivors, with better adjustment to cancer, higher quality of life, and better mental health (Duan-Porter et al., 2016; Matzka et al., 2016; Popa-Velea et al., 2017; Schumacher et al., 2015; Wenzel et al., 2002; Ye et al., 2017). More specifically, high-resilience patients reported less anxiety and depression; higher physical, emotional, and social functioning; and a better quality of life than low-resilience patients (Schumacher et al., 2015). Somasundaram and Devamani (2016) find that resilience was significantly associated with less hopelessness and less hopelessness can be linked to coping.

There is literature (Ristevska-Dimitrovska et al. (2015). that suggest depression is negatively correlated with resilience, which highlights the complexity of defining psychological resilience

An interesting finding on the benefits of resilience in mental health outcomes is that the benefits are not only the identified benefits of “high” resilience but also the magnitude of the benefits. Lam et al. (2012) for example found in their study analysing distress of breast cancer patients that benefits of “high” resilience could be identified up to 6 years after the diagnosis. For example women with stable low levels of distress over the first 8 months post-operatively (identified as a resilient group) had the best 6-year psychosocial outcomes while women who experienced distress at 8 months had significantly greater longer-term psychological distress, cancer-related distress, and poorer social adjustment after 6 years.

2.2 Resilience and somatic symptoms, medical compliance and survival rate

Although we found no studies that would directly link higher levels of resilience to cancer survival, there are indications that resilience is linked to clinical outcomes in non-cancer related treatment (Trinh et al., 2021; Rojas et al.,2018; DeNisco et al. 2011) and that the negative impact of treatment during treatment is lesser. As for cancer treatment the severity of more negative symptoms such as; fatigue, nausea and vomitus, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea have been found to be in negative correlation with resilience (Ristevska-Dimitrovska et al., 2015; Zou et al., 2018). Resilience has also been linked in a study by Molina et al. (2014) to improve adherence to care guidelines.

Furthermore, although there are no studies as of yet, indicating a link with resilience and cancer survival, resilience has been reported to influence physical health in general. For example, resilience was found as a protective effect against coronary heart disease in a 10-year study of 1,306 men (Kubzansky et al., 2001) as well as against chronic illness in adults (Becker and Newsom, 2005) and children (Vinson, 2002), and in helping avoid the onset of illness (Yi, Smith, and Vitaliano, 2005).

2.3 Who benefits of resilience?

Patient specific benefits of resilience have been identified in spite of sex or race (Lau et al., 2020). However, generalisability across cancer stages, sociodemographic or cultural factors seem to not have been investigated.

Lau et al. (2020) also concluded that benefits of resilience could be found across age groups, but particularly long-term mental health benefits and also a link to societal benefit has been made in studies on adolescents and young adults. Rosenberg et al. (2014) found that resilience was connected to stress and coping; goals, purpose, and planning; optimism; gratitude and meaning; and connection and belonging for patients with a mean age of 17 years. The same study concluded that benefits of resilience improved long-term psychosocial outcomes, supporting findings by Fernandez et al. (2011) connecting resilience of adolescents and young adults with cancer to long term societal benefits.

However, benefits of resilience also for older patients have been identified by Matzka et al. (2014). Older cancer patients with higher resilience, experience lower psychological distress and were found physically more active.

Although the body of literature on resilience seems to focus on the patient and not so much on the societal level, there are studies broadening the understanding of resilience outside of the patient. A body of literature have for example analysed the care-givers levels of resilience, finding correlations between care-givers resilience and well-being (Bajjani-Gebara et al.,2019). Although literature could not be found on care giver or family member resilience levels and patient well-being, authors call for further investigating on the concept of family-resilience as well resilience as a dyadic relationship (Gibbons et al., 2019; Lillie et al., 2018; Li et al., 2018). Chapter 4 further expands the benefits of resilience to a societal level.

What needs to be noted and what is reviewed in d21. and 2.2 is that there is not one but several definitions of reliance and that the understanding of resilience difference in previous literature. The working definition in BOUNCE is that: "Resilience is a conglomerate of dynamic self-regulatory capacities that allow to mobilize and use internal and external resources over time in the face of adversity in order to maintain or promote wellbeing. The construct of resilience is used in three ways: (a) Resilience as a personal capacity or potential; (b) Resilience as a post trauma adaptive process or trajectory; (c) Resilience as an outcome of maintaining healthy functioning and subjective well-being despite exposure to adversity. In this deliverable, for the purpose of quantifying the benefits of resilience, the construct of resilience as an outcome (c) is in focus.

3. BOUNCE Stakeholder understanding of the benefits of resilience for breast cancer patients

BOUNCE Stakeholders were identified in WP 1 and stakeholders have been interacted with throughout BOUNCE. Through semi-structured interviews BOUNCE stakeholders have identified potential benefits of resilience and the particular benefits of strengthening of resilience. The stakeholder understanding was developed via semi-structured individual interviews as well as focus group interviews. The stakeholder mapping has been previously presented in WP 1 and the findings from the stakeholder interviews related to benefits of resilience and benefits of strengthening resilience are presented here. Altogether 102 number of respondents were heard. The responses were analysed with content analysis and categorized into different themes and subthemes.

Table 1, Benefits of resilience identified by BOUNCE stakeholders

Stakeholder	**Benefit**
Health and social service providers	● Deeper understanding of patients' reactions to stress and treatments ● Supporting patients to get back to work and providing suggestions for suitable workload ● Fewer concerns from the patients after the treatments ● Appropriate allocation of resources

Patient	● Reduced fears ● Better self-esteem ● Making better decisions regarding work and family life ● Better understanding on one's own resources and how to better adapt to the illness
Family (husband/partner, relatives)	● Being able to cope better in everyday life
Employer	● Reduced sick leave day
Authorities, governments and policy makers, authorities)	● Improved quality of life for the relevant citizens (patient, family)
Financial service providers insurers, charities, foundations of health & social care)	● Better quality of life for breast cancer patients ● Potential cost savings from reduced use of inefficient services or service use and sick leaves caused by low resilience

All BOUNCE stakeholder groups could identify in interviews benefits of resilience and benefits of strengthening the resilience of breast cancer patients during the cancer treatment. Table 1 presents the compiled findings from the stakeholder interviews. The main benefits of strengthening resilience as identified by patients in in Finland, Italy and Portugal are better self-esteem, reduced fears, better decision making and better adaptation to illness. The benefits as identified by the other stakeholders are better quality of life and better coping (identified by family members) of the patient with effects cascading to reduced sick-leaves (identified by employer).

The following chapter will present a literature review on resilience strengthening interventions and the found impact or benefit thereof.

3. Enhancing resilience of breast cancer patients with interventions

In d2.1 and 2.2. resilience and the definition and understanding of resilience was sought for but in 2.3 the benefits of resilience and particularly the benefits of strengthening resilience is analysed via literature on strengthening interventions.

3.1. Literature review on interventions to strengthen resilience

A literature review was conducted in 2019 to enhance the multifaceted understanding of the benefits of resilience and the possibilities to strengthen resilience. Two databases were searched: Ovid (Medline) and Cinahl for years from 1998 to 2019. We searched for studies with female breast cancer patients of all ages and included studies with early breast cancer and adjuvant therapy. Only systematic reviews and meta-analysis exploring intervention studies were included as the number of relevant citations was thousands and we decided to concentrate on publications that had gathered and summarised the evidence in order to get a holistic view of literature on the past 20 years rather than restricting the timeline on our review.

Studies with late-stage cancer patients or metastatic breast cancer patients were excluded.

Search terms included breast cancer, intervention and different possible outcomes for intervention studies. A search was conducted related to strengthening resilience through interventions and since resilience is a combination of several psychosocial factors, the key word search conducted was not limited to the term resilience but included resilience as well as adaptation, quality of life and wellbeing. The search terms for each database are presented in table 2 and 3.

Table 2. Search terms for Ovid (Medline)

Ovid (Medline)	
No	**Search term**
1	Breast cancer.mp OR exp. Breast Neoplasms/
2	intervention.mp
3	exp RESILIENCE, PSYCHOLOGICAL/ OR resilience.mp
4	exp Adaptation, Psychological/
5	adaptation.mp
6	quality of life.mp OR exp “Quality of Life”/
7	Stress, Psychological/

8	wellbeing.mp
9	empowerment.mp OR exp “Power (Psychology)*/
10	functionality.mp
11	recovery.mp
12	3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11
13	1 AND 2 AND 12
14	limit 13 to (evaluation studies OR guideline OR meta-analysis OR practice guideline OR “review” OR “scientific integrity review” OR systematic reviews OR validation studies)
15	limit 14 to yr.=”1998-Current”

Table 3. Search terms for Cinahl

Cinahl	
No	**Search term**
1	(MH “Breast Neoplasms”)
2	“Breast cancer”
3	S1 OR S2
4	(MH Nursing Interventions”) OR (MH “Intervention Trials”) OR “intervention” OR (MH “Experimental Studies+”)
5	“resilience”
6	(MH “Adaptation, Psychological+”) OR “Adaptation”
7	(MH “Quality of Life+”) OR “quality of life”
8	(MH “Stress+”) OR “stress” OR (MH “Stress Disorders, Post Traumatic+”)
9	“wellbeing”

10	(MH “Empowerment”) OR “empowerment” OR (MH “Power+”)
11	S5 OR S6 OR S7 OR S8 OR S9 OR S10
12	S3 AND S4 AND S11

In total, 287 articles were found, but based on title, abstract and full text screening 50 articles were included in this report. Flow chart of the literature search as figure 1.

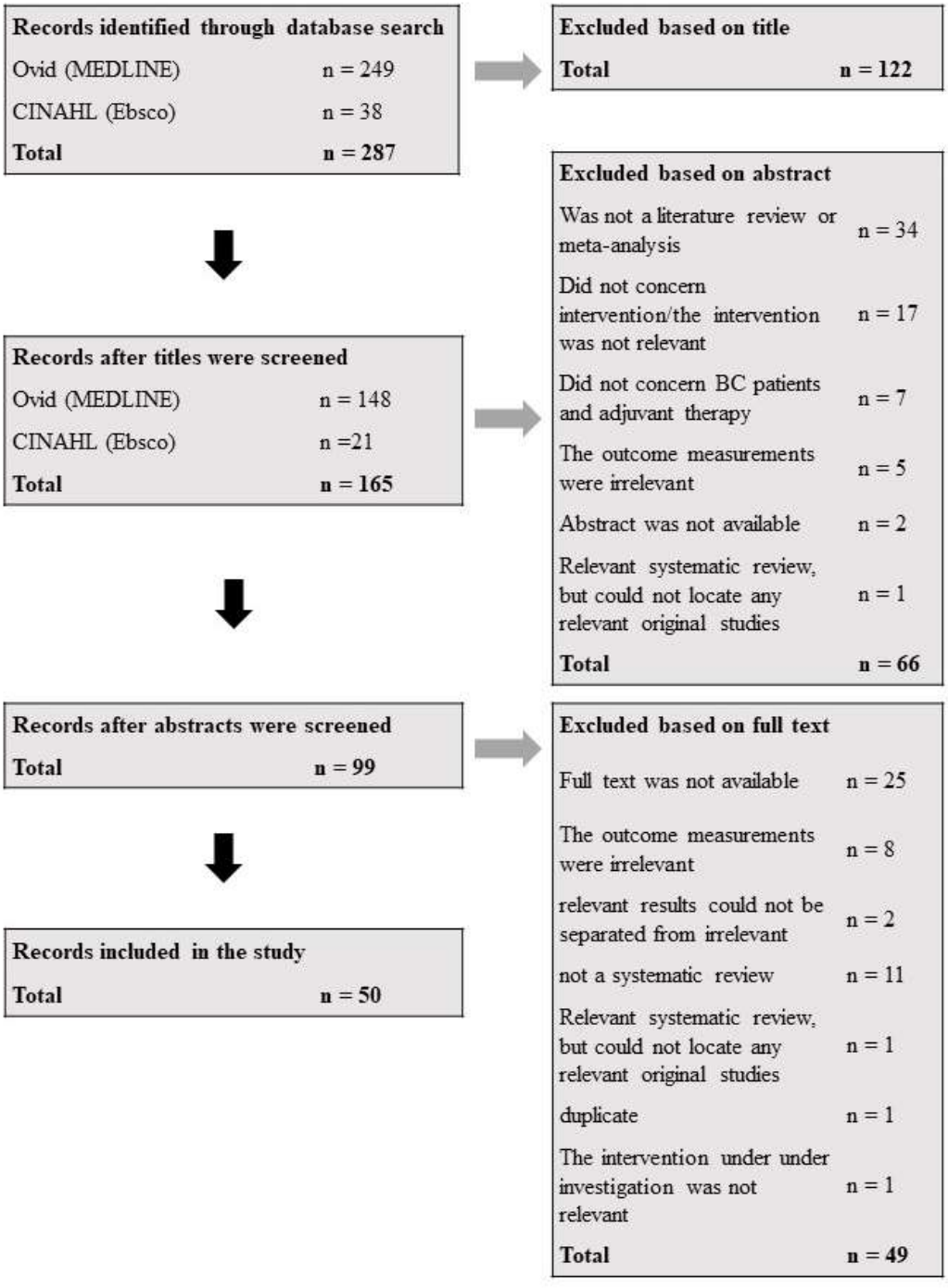

Fig. 1. Flow chart of the literature search

3.3. Results of the literature review- benefits of resilience strengthening interventions

Several different types of interventions have been studied to increase breast cancer patients' resilience. We have divided the interventions found in the literature review into four different categories: 1) digital support, 2) physiotherapy and exercises, 3) psychological interventions

and 4) spiritual, alternative and complementary interventions such as yoga, mindfulness, Pilates, acupuncture, massage therapy, creative therapy etc. Digital support consists of interventions such as online training and education, such as e-learning course on coping. Physiotherapy and exercises consist of interventions such as stretching as well as aerobic exercises. Psychological interventions consist of interventions such as Cognitive behavioural therapy and stress management training. Spiritual, alternative and complementary interventions consist of interventions such as relaxation, visualisation, writing therapy.

Table 5, Literature review on resilience strengthening interventions results

	Authors	**Title**	**Journal outlet**
1	Bluethmann SM, Vernon SW, Gabriel KP, Murphy CC, Bartholomew LK	Taking the next step: a systematic review and meta-analysis of physical activity and behaviour change interventions in recent post-treatment breast cancer survivors. [Review]	Breast Cancer Research & Treatment. 149(2):331-42, 2015 Jan
2	Brandao T, Schulz MS, Matos PM	Psychological intervention with couples coping with breast cancer: a systematic review. [Review]	Psychology & Health. 29(5):491-516, 2014
3	Buffart LM, van Uffelen JG, Riphagen II, Brug J, van Mechelen W, Brown WJ, Chinapaw MJ	Physical and psychosocial benefits of yoga in cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials. [Review]	BMC Cancer. 12:559, 2012 Nov 27
4	Carayol M, Bernard P, Boiche J, Riou F, Mercier B, Cousson-Gelie F, Romain AJ, Delpierre C, Ninot G	Psychological effect of exercise in women with breast cancer receiving adjuvant therapy: what is the optimal dose needed? [Review]	Annals of Oncology. 24(2):291-300, 2013 Feb
5	Carayol M, Delpierre C, Bernard P, Ninot G	Population-, intervention- and methodology-related characteristics of clinical trials impact exercise efficacy during adjuvant therapy for breast cancer: a meta-regression analysis.	Psycho-Oncology. 24(7):737-47, 2015 Jul
6	Casellas-Grau A, Font A, Vives J	Positive psychology interventions in breast cancer. A systematic review. [Review]	Psycho-Oncology. 23(1):9-19, 2014 Jan
7	Cheema, Bobby	Progressive resistance training in breast cancer: a systematic review of clinical trials. [Review] [52 refs]	Breast Cancer Research & Treatment. 109(1):9-26, 2008 May

8	Cramer H, Lange S, Klose P, Paul A, Dobos G	Yoga for breast cancer patients and survivors: a systematic review and meta-analysis. [Review]	BMC Cancer. 12:412, 2012 Sep 18
9	Cramer H, Lauche R, Klose P, Lange S, Langhorst J, Dobos GJ	Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. [Review]	Cochrane Database of Systematic Reviews. 1:CD010802, 2017 01 03
10	D'Abramo F, Goerling U, Guastadisegni C	Targeted drugs and Psycho-oncological intervention for breast cancer patients. [Review]	Journal of Negative Results in Biomedicine. 15:6, 2016 Apr 01
11	de Boer AG, Taskila TK, Tamminga SJ, Feuerstein M, Frings-Dresen MH, Verbeek JH	Interventions to enhance return-to-work for cancer patients. [Review][Update of Cochrane Database Syst Rev. 2011;(2):CD007569; PMID: 21328297]	Cochrane Database of Systematic Reviews. (9):CD007569, 2015 Sep 25
12	Duijts SF, Faber MM, Oldenburg HS, van Beurden M, Aaronson NK	Effectiveness of behavioral techniques and physical exercise on psychosocial functioning and health-related quality of life in breast cancer patients and survivors--a meta-analysis. [Review]	Psycho-Oncology. 20(2):115-26, 2011 Feb
13	Fors EA, Bertheussen GF, Thune I, Juvet LK, Elvsaas IK, Oldervoll L, Anker G, Falkmer U, Lundgren S, Leivseth G	Psychosocial interventions as part of breast cancer rehabilitation programs? Results from a systematic review. [Review]	Psycho-Oncology. 20(9):909-18, 2011 Sep
14	Galvao, Daniel A.	Review of exercise intervention studies in cancer patients. [Review] [96 refs]	Journal of Clinical Oncology. 23(4):899-909, 2005 Feb 01
15	Greenlee H, Balneaves LG, Carlson LE, Cohen M, Deng G, Hershman D, Mumber M, Perlmutter J, Seely D, Sen A, Zick SM, Tripathy D, Society for Integrative Oncology	Clinical practice guidelines on the use of integrative therapies as supportive care in patients treated for breast cancer. [Review][Erratum appears in J Natl Cancer Inst Monogr. 2015 May;2015(51):98; PMID: 26063898]	Journal of the National Cancer Institute. Monographs. 2014(50):346-58, 2014 Nov
16	Haller H, Winkler MM, Klose P, Dobos G, Kummel S, Cramer H	Mindfulness-based interventions for women with breast cancer: an updated systematic review and meta-analysis. [Review]	Acta Oncologica. 56(12):1665-1676, 2017 Dec

17	Hoving JL, Broekhuizen ML, Frings-Dresen MH	Return to work of breast cancer survivors: a systematic review of intervention studies. [Review] [44 refs]	BMC Cancer. 9:117, 2009 Apr 21
18	Hulett JM, Armer JM	A Systematic Review of Spiritually Based Interventions and Psychoneuroimmunological Outcomes in Breast Cancer Survivorship. [Review]	Integrative Cancer Therapies. 15(4):405-423, 2016 12
19	Jassim GA, Whitford DL, Hickey A, Carter B	Psychological interventions for women with non-metastatic breast cancer. [Review]	Cochrane Database of Systematic Reviews. (5):CD008729, 2015 May 28
20	Lee MS, Choi TY, Ernst E	Tai chi for breast cancer patients: a systematic review. [Review] [29 refs]	Breast Cancer Research & Treatment. 120(2):309-16, 2010 Apr
21	Lee PL, Tam KW, Yeh ML, Wu WW	Acupoint stimulation, massage therapy and expressive writing for breast cancer: A systematic review and meta-analysis of randomized controlled trials.	Complementary Therapies in Medicine. 27:87-101, 2016 Aug
22	Lipsett A, Barrett S, Haruna F, Mustian K, O'Donovan A	The impact of exercise during adjuvant radiotherapy for breast cancer on fatigue and quality of life: A systematic review and meta-analysis. [Review]	Breast. 32:144-155, 2017 Apr
23	Loughney L, West MA, Kemp GJ, Grocott MP, Jack S	Exercise intervention in people with cancer undergoing neoadjuvant cancer treatment and surgery: A systematic review. [Review]	European Journal of Surgical Oncology. 42(1):28-38, 2016 Jan
24	Matchim, Yaowarat	Measuring the psychological impact of mindfulness meditation on health among patients with cancer: a literature review. [Review] [41 refs]	Oncology Nursing Forum. 34(5):1059-66, 2007 Sep
25	Matsuda A, Yamaoka K, Tango T, Matsuda T, Nishimoto H	Effectiveness of psychoeducational support on quality of life in early-stage breast cancer patients: a systematic review and meta-analysis of randomized controlled trials. [Review]	Quality of Life Research. 23(1):21-30, 2014 Feb
26	McNeely, Margaret L	Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis.	CMAJ Canadian Medical Association Journal. 175(1):34-41, 2006 Jul 04
27	Naaman SC, Radwan K, Fergusson D, Johnson S	Status of psychological trials in breast cancer patients: a report of three meta-analyses. [Review] [64 refs]	Psychiatry. 72(1):50-69, 2009
28	Oldervoll, L M.	Physical exercise results in the improved subjective well-being of a few or is effective rehabilitation for all cancer patients?. [Review] [49 refs]	European Journal of Cancer. 40(7):951-62, 2004 May

29	Pan YQ, Yang KH, Wang YL, Zhang LP, Liang HQ	Massage interventions and treatment-related side effects of breast cancer: a systematic review and meta-analysis.	International Journal of Clinical Oncology. 19(5):829-41, 2014 Oct
30	Pinto, Bernardine M	Methodologic issues in exercise intervention research in oncology. [Review] [59 refs]	Seminars in Oncology Nursing. 23(4):297-304, 2007 Nov
31	Post KE, Flanagan J	Web based survivorship interventions for women with breast cancer: An integrative review. [Review]	European Journal of Oncology Nursing. 25:90-99, 2016 Dec
32	Ryhanen AM, Siekkinen M, Rankinen S, Korvenranta H, Leino-Kilpi H	The effects of Internet or interactive computer-based patient education in the field of breast cancer: a systematic literature review. [Review] [35 refs]	Patient Education & Counseling. 79(1):5-13, 2010 Apr
33	Shneerson C, Taskila T, Gale N, Greenfield S, Chen YF	The effect of complementary and alternative medicine on the quality of life of cancer survivors: a systematic review and meta-analyses. [Review]	Complementary Therapies in Medicine. 21(4):417-29, 2013 Aug
34	Short CE, James EL, Stacey F, Plotnikoff RC	A qualitative synthesis of trials promoting physical activity behaviour change among post-treatment breast cancer survivors. [Review]	Journal of Cancer Survivorship. 7(4):570-81, 2013 Dec
35	Smith KB, Pukall CF	An evidence-based review of yoga as a complementary intervention for patients with cancer. [Review] [45 refs]	Psycho-Oncology. 18(5):465-75, 2009 May
36	Spence RR, Heesch KC, Brown WJ	Exercise and cancer rehabilitation: a systematic review. [Review] [30 refs]	Cancer Treatment Reviews. 36(2):185-94, 2010 Apr
37	Stricker, Carrie Tompkins.	Evidence-based practice for fatigue management in adults with cancer: exercise as an intervention. [Review] [57 refs]	Oncology Nursing Forum. 31(5):963-76, 2004 Sep
38	Tsimopoulou I, Pasquali S, Howard R, Desai A, Gourevitch D, Tolosa I, Vohra R	Psychological Prehabilitation Before Cancer Surgery: A Systematic Review. [Review]	Annals of Surgical Oncology. 22(13):4117-23, 2015 Dec
39	Van Dijck S, Nelissen P, Verbelen H, Tjalma W, Gebruers N	The effects of physical self-management on quality of life in breast cancer patients: A systematic review. [Review]	Breast. 28:20-8, 2016 Aug
40	Zainal NZ, Booth S, Huppert FA	The efficacy of mindfulness-based stress reduction on mental health of breast cancer patients: a meta-analysis. [Review]	Psycho-Oncology. 22(7):1457-65, 2013 Jul

41	Zeng Y, Huang M, Cheng AS, Zhou Y, So WK	Meta-analysis of the effects of exercise intervention on quality of life in breast cancer survivors.	Breast Cancer. 21(3):262-74, 2014 May
42	Zhang J, Xu R, Wang B, Wang J	Effects of mindfulness-based therapy for patients with breast cancer: A systematic review and meta-analysis. [Review]	Complementary Therapies in Medicine. 26:1-10, 2016 Jun
43	Zhang J, Yang KH, Tian JH, Wang CM	Effects of yoga on psychologic function and quality of life in women with breast cancer: a meta-analysis of randomized controlled trials. [Review]	Journal of Alternative & Complementary Medicine. 18(11):994-1002, 2012 Nov
44	Zhu J, Ebert L, Wai-Chi Chan S	Integrative Review on the Effectiveness of Internet-Based Interactive Programs for Women With Breast Cancer Undergoing Treatment. [Review]	Oncology Nursing Forum. 44(2):E42-E54, 2017 Mar 01
45	Zou LY, Yang L, He XL, Sun M, Xu JJ	Effects of aerobic exercise on cancer-related fatigue in breast cancer patients receiving chemotherapy: a meta-analysis.	Tumour Biology. 35(6):5659-67, 2014 Jun
46	Haller, H., Winkler, M. M., Klose, P., Dobos, G., Kuemmel, S., & Cramer, H.	Mindfulness-based interventions for women with breast cancer: an updated systematic review and meta-analysis.	Acta oncologica 56.12, 2017, 1665-1676.
47	Browall, M., Forsberg, C., & Wengström, Y.	Assessing patient outcomes and cost-effectiveness of nurse-led follow-up for women with breast cancer - have relevant and sensitive evaluation measures been used?	Journal of clinical nursing, 26(13-14), 2017, 1770-1786.
48	Andria Syka, R. N.	The Effect of Exercise in Surviving Patients with Breast Cancer: A Systematic Review. Benefits of resilience- Cost-benefit model	International Journal of Caring Sciences, 8(2), 2015, 488.
49	Galantino, M. L., Cannon, N., Hoelker, T., Iannaco, J., & Quinn, L.	Potential benefits of walking and yoga on perceived levels of cognitive decline and persistent fatigue in women with breast cancer.	Rehabilitation Oncology, 25(3), 2007, 3.

As for digital support interventions, the results in the studies identified in the literature review showed positive results. For example, Zhu et al 2017 stated that 3 months after an intervention an effect on positive coping and reduced negative emotions. Zhu et al. (2017) could also identify significant decrease in depression among breast cancer patients three months after an online comprehensive health enhancement support system intervention. Zhu et al (2017) also reported several studies (Shaw et al., 2017, Huang et al., 2011) showing significant benefits from online support programmes. However, Salzer et al. 2010 (in Zhu et al., 2017) found no significant benefits on Quality of Life (QOL) from unmoderated online support programmes.

Digital support	
Intervention	**Results**
Internet-based interactive programs	Significantly improved emotional processing and positive coping, reduced negative emotions at five months and decreased depression among women with breast cancer at three months). Inconsistent results regarding the impact on QOL. *Zhu et al. 2017.*

As for Physiotherapy, in the literature review we found studies on interventions such as stretching, resistance training, aerobic exercise, low-intensity mind-body exercises and (general) exercises. For stretching and combined aerobic-resistance exercise interventions, significant results could be found not on QOL, but on the reduction of fatigue (Lipsett et al. 2017; Hulett and Armer 2016). Post and Flanagan (2016) identified significant benefits of a (general) exercise intervention on QOL, while other studies analysing exercise seemed to find a moderate to large-sized, but not significate, impact on QOL (Lipsett et al. 2017). However, Lee et al. (2014) reported a physical activity and lifestyle intervention study with significant improvements in QOL measures for the intervention group as compared to control groups. Furthermore, for resistance training, combined aerobic resistance training, and low-intensity mind-body exercise interventions no significant impact on QOL could be found (Lipsett et al. 2017).

Physiotherapy and sport activities	
Intervention	**Results**
Stretching	Decrease in fatigue. *(Hulett and Armer 2016)*
Resistance training	Small-sized but non-significant reduction in fatigue in favour of the exercise group. *(Lipsett et al. 2017)*
Combined aerobic-resistance exercise	Medium-sized and significant reduction in fatigue. *(Lipsett et al. 2017)*
Low-intensity mind-body exercise	Large sized but non-significant reduction in fatigue in favour of the exercise group with large statistical heterogeneity. *(Lipsett et al. 2017)*
Home-based aerobic exercise	Medium-sized but non-significant reduction in fatigue in favour of the exercise group with no statistical heterogeneity. *(Lipsett et al. 2017)*
Exercise	Large-sized but non-significant improvement in QOL in favour of the exercise group. *(Lipsett et al. 2017)*

	Two physical activity and lifestyle intervention studies had significant improvements in QOL measures for the intervention as compared to control groups. (Lee et al., 2014)

As for cognitive behavioural therapy Post and Flanagan (2016) reported significant improvements on self-efficacy, fatigue and distress as compared to a control group in 3 out of 4 in the literature review included intervention studies. Furthermore, Hulett and Armer (2016) reported decreased depression, decreased anxiety, decreased stress and increased relaxation in an intervention study on Cognitive based stress management.

Psychological interventions (patient education, psychological support, therapy)	
Intervention	**Results**
CBSM (cognitive-based stress management)	Decreased depression, anxiety and stress. Increased stress. *(Hulett and Armer 2016)*
Cognitive behavioral therapy	Improvements for self-efficacy, fatigue and distress. *(Post and Flanagan 2016)*

As for spiritual, alternative and complementary interventions, positive significant impact was reported for mindfulness interventions as well for Qigong (Hulett and Amber, 2016) as increased QOL, decreased depression and fatigue. As for other alternative interventions such as yoga, acupuncture, massage therapy and expressive writing, intervention studies showed differing results.

Spiritual, alternative, complementary interventions (yoga, mindfulness, pilates, acupuncture, massage therapy, creative therapy etc)	
Intervention	**Results**
Yoga	Moderate-quality evidence showing that yoga improved health-related quality of life, reduced fatigue and reduced sleep disturbances in the short term. Yoga did not appear to reduce depression or anxiety in the short term. *(Cramer et al. 2017)* Decreased depression, decreased anxiety, increased Quality of life/vitality/vigor, decreased distress, symptoms, stress and fatigue. *(Hulett and Armer 2016)*
MBSR (mindfulness-	Decreased depression, anxiety, symptoms, stress, rumination,

based stress reduction)	fatigue; Increased QOL, coping, mindfulness, mood and cognitive function. (*Hulett and Armer 2016)*
Qigong	Decrease depression and fatigue; Increased QOL. *(Hulett and Armer 2016)*
RVT (relaxation visualization therapy)	Decrease depression, anxiety, stress. *(Hulett and Armer 2016)*
MBCR (mindfulness-based cancer recovery)	Increase QOL, social support and mood, decrease stress. *(Hulett and Armer 2016)*
BMS (body-mind-spirit)	Increase spiritual growth/spiritual well-being. *(Hulett and Armer 2016)*
Acupuncture	Contradicting results in intervention studies on QOL. No significant change on QoL post-intervention. Reported significant change on depression and decrease in fatigue. *(Lee et al. 2016)*
Massage therapy	Found decrease in anxiety but result for massage therapy and depression showed non-significant results on a study-level. Contradictory results for massage therapy impact on fatigue. *(Lee et al. 2016)*
Expressive writing	Increase in QOL significant. Contradictory results for fatigue and depression. *(Lee et al. 2016)*

4. Preliminary calculation on the patient and societal benefit of resilience strengthening interventions

To demonstrate the benefit of strengthened resilience in breast cancer patients, we conducted preliminary calculations that estimates the monetary and health-related benefits of a resilience strengthening intervention from a societal perspective. In the model we calculate the benefits of a cognitive behavioural therapy, to an average breast cancer patient and compare the results to a no-intervention baseline scenario. The calculation is based on data from BOUNCE as well as data from literature sources.

The health-related benefits were evaluated using Quality of Life (QoL) measures. The QoL data as well as the sick leave data of breast cancer patients were collected from the BOUNCE clinical studies (data collected in WP6 from 4 different pilot centres). During the studies, the patients assessed their QoL using a questionnaire in the beginning and at the end of the 12-month study period. The patients also reported quarterly their sick leave days for the previous

three-month period. The patients did not receive any resilience-strengthening interventions during the study.

From BOUNCE clinical studies, we were able get data for 764 breast cancer patients from which 303 met the inclusion criteria. The inclusion criteria were as follows; both month 0 and month 12 QoL information is available for the patient and sick leave data for at least three of the four data points (M0, M3, M9, M12). For the patients with only three data points for sick leave data, the missing information was generated using the average of sick leaves in the corresponding data point for the patients who met inclusion criteria.

Table 7: description of QoL data from BOUNCE clinical studies

	QoL in month 0	**QoL in month 12**
Mean	0.74	0.76
Median	0.75	0.83
Min	0.25	0.16
Max	1.00	1.00
Standard error	0.19	0.18

Table 8: description of sick leave data from BOUNCE clinical studies

	Sick leaves M0-M3	**Sick leaves M3-M6**	**Sick leaves M6-M9**	**Sick leaves M9-M12**
Mean	39	34	19	13
Median	30	20	2	0
Min	0	0	0	0
Max	100	100	100	92
Standard error	34,8	35,8	29,8	28,7

The data indicates a small increase in QoL as well as a significant decrease in sick leaves for breast cancer patients during a one-year time period even without any resilience-strengthening intervention. Descriptive statistics of the BOUNCE data are demonstrated in tables 7 and 8. The average QoL of breast cancer patients in month 0 was 0.74 and the average QoL in month 12 was 0.76. The average sick leaves for months 0-3 were 39 and the average sick leaves for months 9-12 were 13. Figure 2 depicts visually the expected progression of QoL and sick leaves for breast cancer patients without any resilience-strengthening interventions.

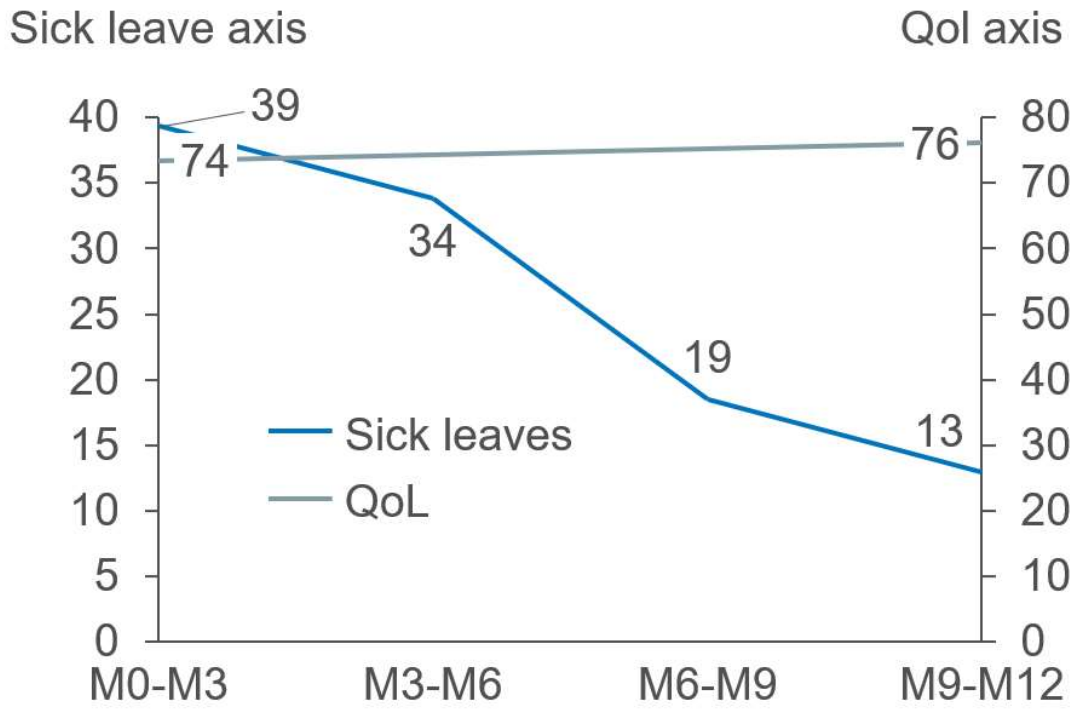

Figure 2: progression of average QoL and average sick leaves of breast cancer patients without intervention in a year

4.1 Benefit for no-intervention and intervention for recovering breast cancer patients- preliminary calculation

The effects of cognitive behavioral therapy on QoL were derived from the literature (Post and Flanagan, 2016; Hulett and Armer, 2016; Jianyin et al., 2013). The impact of patient's improved QoL on the number of sick leaves was estimated from the BOUNCE data using a linear regression model. The model uses the least squares approach to estimate ratio in which sick leaves decrease as QoL score increases. According to the regression model, an increase of 1 point in the patients assessed QoL, results in a decrease of 1,3 sick leave days annually.

The results are depicted in table 9. According to the results, the cognitive behavioural therapy generates 0.05 more health benefits in a year compared to no-intervention, resulting in a QALY of 0.82. In comparison the no-intervention scenario accumulates 0.78 QALY's per year. In addition, the cognitive behavioural therapy is expected to accumulate 12 sick leave days less in a year compared to no-intervention. The sick leaves of a patient with intervention were expected to be 96 days in the 12-month period compared to 108 days with no intervention. This could result in a significant budget impact from the societal perspective.

Table 9: the expected health benefits and sick leaves for no-intervention and intervention for recovering breast cancer patients.

	Health benefits per year, QALY	**Sick leaves**
No intervention	0.78	108
Cognitive behavioural therapy	0.82	96
Change, Δ	+0.05	-12

In conclusion, the results suggest that resilience-strengthening interventions, such as cognitive behavioural therapy in women recovering from breast cancer may lead to a higher quality of life as well as lower costs from the societal perspective in the form of decreased absenteeism. The benefits of improved resilience and resilience trajectory prediction in recovering breast cancer patients will be estimated in more detail in the cost-benefit model included in the WP7 package.

5. Conclusions

In conclusion, research has shown that resilience in cancer patients may buffer against psychological distress and improve quality of life during the disease's trajectory (Ye et al., 2017). The main benefits of strengthening resilience were identified by BOUNCE stakeholders as better self-esteem, reduced fears, better decision making, better adaptation to illness, better quality of life, better coping and reduced sick-leaves. The identified benefits are backed up by literature where benefits such as better adjustment to cancer, higher quality of life, and better mental health and treatment outcomes were identified (Duan-Porter et al., 2016; Matzka et al., 2016; Popa-Velea et al., 2017; Rosenberg et al., 2015; Schumacher et al., 2015; Wenzel et al., 2002; Ye et al., 2017). High resilience or strengthening of resilience is found to have immediate impact, and interventions strengthening resilience can show benefits for patients up to 6 years after diagnosis (Lam et al., 2012).

To date however, there seems to be a gap in research on how to actually promote resilience of breast cancer patients. Interest has however increased in promoting resilience for cancer patients, for example in one study involving patients with advanced-stage cancer, resilience was directly related to higher levels of perceived social support and less hopelessness (Somasundaram at el., 2016). Interventions such as digital support, physiotherapy and exercises, psychological interventions, as well as spiritual, alternative and complementary interventions could detected positive impact. However, the positive impact varied depending on the intervention. In studies on digital interventions improvement on QOL could be found (Zhu et al., 2017). For physiological interventions again the impact was dependent on what kind of physical intervention was in question. As for general exercise positive impact in QOL was reported (e.g., Lipsett et al. 2017). As for psychological interventions, such as cognitive

behavioural therapy, benefits for patients were reported as a decrease in depression and anxiety. For spiritual and alternative interventions again, a decrease in depression could be found for mindfulness-based interventions, Qigong, as well as for relaxation visualization therapy (e.g., Hulett and Armer 2016). Interventions including yoga, expressive writing, massage therapy, or acupuncture studies showed different and sometimes contradictory results regarding impact.

The BOUNCE cost-benefit analysis in task 7.2 is working on quantifying the cost and benefit of a predictive tool of the trajectory of resilience so that future studies to enhance resilience can be implemented. This tool would also take into account the expected quantitative benefits of resilience for a breast-cancer patient and for the society. The preliminary findings indicate that the benefits of receiving interventions - cognitive behavioural therapy in this preliminary calculation - to strengthen resilience for breast cancer patients are higher than the costs for all patients, and that the benefits of interventions targeting patients with low resilience are high for the society as a whole.

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